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SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.

EXAMINER	
ART UNIT	PAPER NUMBER
	6

DATE MAILED:

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☑ This application has been examined ☐ Responsive to communication filed on _____ ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), _____ days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☑ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☑ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☑ Claims 1-9 are pending in the application.

Of the above, claims _____ are withdrawn from consideration.

2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☑ Claims 1-9 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____ has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.
13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

PTOL-326 (Rev. 2-93)

This is a continuation of 08/020,177, now abandoned.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an enabling disclosure. Claims 1-9 are drawn to a method of delivering a gene to the central nervous system of a mammal, comprising administering a neurotropic virus containing a DNA sequence of interest where expression of the DNA sequence of interest is regulated by a latency promoter. It is not apparent from the disclosure that the method would sufficiently deliver a gene to the central nervous system such that the host would receive a benefit from such delivery. Applicant has shown that biologically active β-glucuronidase can be expressed when the DNA sequence for the enzyme operatively linked to the LAT promoter is contained in an HSV vector is administered by corneal abrasion. Although β-glucuronidase is detected, there is no evidence that such expression levels would have an effect on the host mammal. There is no evidence that such expression levels for example correlate to a treatment for a β-glucuronidase deficiency. It is not clear that the delivery of any particular gene or the expression of that gene to any particular level would result in the host having

beneficial effect. Further applicant has not disclosed other neurotropic viruses that can be delivered such that detectable expression of a gene of interest is achieved. Other neurotrophic viruses may not be reach the CNS such that meaningful expression is achieved. Applicant has not shown that any neurotrophic viruses would reach the CNS by other routes of delivery. This is especially problematic as the blood brain barrier would prevent infection by a virus, even one such as HSV. Evidence has not been presented that HSV will infect CNS by say systemic administration via the blood. In addition, applicant has not provided any evidence of promoters other than the LAT promoter that would be effective in the claimed method. For sustained expression, it would seen that latency or a non-reproductive cycle would need to be established. Thus based on applicant's disclosure an undue amount of experimentation would be required of the skilled artisan without a predictable degree of success to implement the invention as claimed.

Claims 1-9 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or

> on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1,2,5 and 6 are rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Dobson et al (1989) J. Virol. 63, 3844-3851. Dobson teaches the delivery of the rabbit ß-globin gene to the CNS of mice where expression of the ß-globin gene is regulated by the HSV-1 latency promoter (page 3850, col. 1, parag. 4, lines 1-6, page 3847, figure 5). The HSV-1 vector is administered by foot pad injection which is a peripheral inoculation (page 344, col. 2, parag. 1, lines 4-6). Thus the claims are clearly anticipated by Dobson.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claims 3,4,7,8 and 9 are rejected under 35 U.S.C. § 103 as being unpatentable over Dobson et al (1989) J. Virol. 63, 3844-3851 in view of Nishimura et al (1986) Proced. Natl. Acad. Sci.

83, 7292-7296. Dobson teaches the delivery of the rabbit ß-globin gene to the CNS of mice where expression of the ß-globin gene is regulated by the HSV-1 latency promoter (page 3850, col. 1, parag. 4, lines 1-6, page 3847, figure 5). The HSV-1 vector is administered by foot pad injection which is a peripheral inoculation (page 344, col. 2, parag. 1, lines 4-6). Dobson does not teach the delivery of β-glucuronidase operatively linked to a promoter. However, Nishimura teaches the DNA sequence for β-glucuronidase. Methods for the insertion of DNA sequence of interest into recombinant HSV-1 vectors as described in Dobson would have been within the scope of skills of the ordinary artisan at the time of the instant invention. Motivation is offered by Dobson in stating that HSV-1 is an vector for the transfer of genes to neurons (page 3850, col. 2, parag. 3, lines 1-2) Thus it would have been obvious to the ordinary artisan at the time of the instant invention to insert a DNA sequence of choice into an HSV-I vector where expression of said sequence is regulated by the HSV-I LAT promoter, infect mammals with said vector to deliver and express the heterologous DNA sequences in the central nervous system of the mammal. For mere delivery as claimed the cited prior offers a reasonable expectation of success.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Crouch, Ph.D. whose telephone number is (703) 308-1126.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Deborah Crouch

Dr. D. Crouch
March 28, 1996